

Case Report

McCune-Albright syndrome without endocrine dysfunction: Case report in a young boy

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ABSTRACT

The McCune-Albright syndrome (MAS) is a sporadic rare disease characterized by a triad of physical signs: Café-au lait spots, polyostotic fibrous dysplasia, and autonomous endocrine hyperfunction. Based on the studies, it can be concluded that this syndrome is caused by mutations that happen in the gene: GNAS1. A small number, but not all, of the patient's cells contain this faulty gene (mosaicism). MAS is predominantly observed in girls and is rarely reported in males. We report a 5-year-old boy with café-au-lait spots, polyostotic fibrous dysplasia, and without any endocrine dysfunction.

Key words: *Fibrous dysplasia, McCune-Albright syndrome, Polyostotic*

McCune-Albright syndrome (MAS) described in 1937 by Donovan James McCune and Fuller Albright [1,2]. MAS occurs in 1 in 100,000 to 1 in 1,000,000 people worldwide. The classical triad of MAS consists of polyostotic fibrous dysplasia (PFD), skin hyperpigmentation (café-au-lait spots), and endocrine dysfunctions [3]. Any combination of two or more of these typical findings constitutes MAS. Patients with MAS display mosaicism of activating somatic mutations of the gene encoding the alpha-subunit of Gs (GNAS1) [4]. Fibrous dysplasia (FD) lesions are typically found in the long bones of the extremities, rarely found in the hands, feet, or spine [5-8], ranging from asymptomatic lesions to the one causing marked disfigurement of the skull and spine [9]. Involvement of the skull can be particularly problematic, with lesions of the orbit resulting in visual loss or proptosis and lesions of the ear resulting in deafness and vertigo.

The café-au-lait spots are one of the most obvious signs of MAS and present as single or multiple tan-brown hyperpigmented flat macules with irregular ("coast of Maine") borders developing during infancy and becoming even more obvious with age or with sun exposure [1]. The most common form of autonomous endocrine hyperfunction in this syndrome is gonadotropin-independent precocious puberty. However, the non-endocrine abnormalities include chronic liver disease, tachycardia, and rarely sudden death, possibly from cardiac arrhythmias.

CASE REPORT

A 5-year-old Asian boy presented to pediatric ED with acute exacerbation of asthma which was managed as per hospital protocol. On examination, he was noted to have multiple café au lait

spots across the left side of his body affecting his chest and back and left upper limb (Fig. 1). According to parents, these features have been present since he was a young baby. Previously, he was reviewed by a dermatologist at approximately 8 months of age and diagnosed as having eczema, leading to post-inflammatory skin infiltrates which were treated with emollients and steroid ointments with not much benefit. During this admission, he had a chest X-ray done to further investigate his respiratory illness, in which an incidental finding of a lytic lesion in the left humerus (Fig. 2) was noticed.

On physical examination, his weight was 15.3 kg (just above the 10th centile) and his height was 105 cm (above 25th centile for his age) and approximately at the mid-parental percentile for his family height. In view of café au lait macules and lytic bone lesions, a diagnosis of MAS was considered, and a battery of endocrine investigations was performed. An endocrinologist opinion was also assisted, and genetic testing for GNAS gene was done which showed no evidence of mosaicism.

Blood investigations revealed the following results: Glucose: 4.8(3.9–7.8) mmol/L, hemoglobin A1c (HbA1c):HbA1c IFCC: 31 (19–40) mmol/mol and HbA1c DCCT derived: 5.0% (3.9–5.8%), CRP: <5 (0–5 mg/dl), calcium: 2.51 (2.20–2.70) mmol/L, phosphorus: 1.11 (1.05–1.80) mmol/L, liver profile: Normal, creatinine: 35(23–37) µmol/L, thyroid profile: T4 16.2 (12–22) pmol/L, TSH 4.80 (0.27–4.20), thyroid peroxidase Ab: <4 IU/ml(Negative), growth hormone (GH) (random): 0.3 ng/ml, IGF-1: 8.3 (5.8–29.5) nmol/L, testosterone: <0.1 (0.1–1.1) nmol/L, prolactin: 7.29 (4–15.2) ng/ml, FSH: Lo 0.71 (1.5–12.4) mIU/ml, and LH levels were low: <0.10 (1.7–8.6) mIU/ml.

X-ray chest/skeletal survey reported FD of proximal left humerus, outer aspect of left clavicle, and also in the scapula



Figure 1: Café au lait spots over left side of body



Figure 2: Fibrous dysplasia of proximal humerus and clavicle

adjacent to the lower border of globoid fossa. According to the criteria, the diagnosis of MAS was confirmed. At present, as the child has no associated endocrinal abnormalities, he was kept under follow-up to have a close eye on his growth and to detect early any associated endocrinal dysfunction. He has also been referred to orthopedic surgeon in view of the bony lytic lesions.

DISCUSSION

Our child had unilateral café-au-lait spots and PFD without any endocrine manifestations. PFD is a distinctive finding in affected individuals. It refers to cases in which multiple skeletal sites are affected and it often predominates on one side of the body (unilateral) [5] which was similar in our case. The prevalence of café-au-lait spots in MAS was estimated to range from 53.1% to 92.5% [3]. These lesions are often limited to one side of the body, which usually corresponds to the side with bone involvement and generally do not cross the midline. Moreover, they are typically arranged in a segmental pattern, which follows the developmental lines of Blaschko [6].

Diagnosis of MAS is usually established on clinical grounds. Plain radiographs are often sufficient to make the diagnosis of FD. The explanation which is widely accepted but remains unproven

for the lack of vertical transmission, along with the observation that the skin and bone lesions tend to lateralize, is that the disease results from postzygotic mutations; therefore, the patients are referred to as somatic mosaics - the mosaicism could explain the varied clinical picture of those with this syndrome [7], and more so, a negative result from readily available (but unaffected) tissue does not exclude the presence of the mutation.

The most important aspect of genetics is counselling of families to assure that there is no vertical transmission of the disease, and therefore, parents need not feel “responsible,” and patients can be assured that they will not transmit the disease to their offspring [8]. However, several laboratory studies should be conducted during the follow-up period to investigate for any of the endocrinological dysfunction, the most common being gonadotropin-independent precocious puberty, also hyperthyroidism [10], hypercortisolism [11], and/or pituitary adenomas-secreting GH and/or prolactin [12]. Hypophosphatemic osteomalacia has also been reported [13].

No specific medications are available to treat the bone manifestations of MAS. Antiresorptive agents (e.g., alendronate and its congeners [bisphosphonates]) are being evaluated for this indication and have great palliative value owing to their pain-controlling attributes in this disease. The precocious puberty of MAS generally does not respond to gonadotropin-releasing hormone (GnRH) agonists, and short-acting aromatase inhibitors have had limited effectiveness. Inconsistent results have been reported with bromocriptine, cabergoline, octreotide, or a combination of these. Pegvisomant, a GH receptor antagonist, is a possibility, though it has not been specifically evaluated for the treatment of MAS with GH pathology [14]. There are no known environmental, ethnic, or geographic risk factors for the development of MAS. So far, all cases of MAS are sporadic. Symptoms begin during childhood, though in some cases, the disease is clinically silent and is discovered on routine radiographs obtained for an unrelated reason [15]. The history and the physical examination can vary based on a specific person's syndrome.

CONCLUSION

MAS is a multisystemic condition with a host of variable presentations. Diagnosis and treatment of this syndrome require a high index of suspicion in any patient with characteristic café-au-lait spots and endocrine dysfunction or pathologic fractures. No measures are available to prevent MAS; however, appropriate care must be taken for fracture prevention in patients with severe PFD.

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